Treating the chronic wound: A practical approach to the care of nonhealing wounds and wound care dressings

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Chronic wounds are a major healthcare problem costing the United States billions of dollars a year. The American Academy of Dermatology has underscored the significance of wound care in dermatological practice. It is critical for all dermatologists to understand the elements of diagnosis and therapy. We emphasize major aspects of diagnosis and present a simple classification of wound dressings with guidelines for usage and relative cost data. (J Am Acad Dermatol 2008;58:185-206.)

Learning objective: After completing this learning activity, participants should be able to diagnose common types of chronic wounds, formulate a therapeutic plan, and describe the major classes of topical therapies and dressings for the chronic wound.

A chronic wound is defined as a break in the skin of long duration (>6 weeks) or frequent recurrence.[1,2] In today's society, chronic wounds represent a major health care burden. Approximately 1% to 2% of individuals will be affected by leg ulceration during their lifetime, and this figure will likely increase as the population ages.[3-5] The associated costs are staggering. A recent article suggests that treatment costs for venous ulcers alone approach $3 billion, accounting for a substantial portion of the total health care budget.[6] Global wound care expenditures amount to $13 to $15 billion annually.[7]

A myriad of factors can delay wound healing. Chronic disease, vascular insufficiency, diabetes, neurologic defects, nutritional deficiencies, advanced age, and local factors such as pressure, infection, and edema can all impair healing. Wound care is a holistic endeavor that requires an accurate identification of the specific entities interfering with wound healing in a particular patient.

Abbreviations used:	
ABI:	ankle-brachial index
CMC:	carboxymethylcellulose
CRP:	C-reactive protein
ESR:	erythrocyte sedimentation rate
MRI:	magnetic resonance imaging
MRSA:	methicillin-resistant *Staphylococcus aureus*
PG:	pyoderma gangrenosum
rhPDGF:	recombinant human platelet-derived growth factor
TBI:	toe-brachial index
TNP:	topical negative pressure
VAC:	vacuum-assisted closure
VEGF:	vascular endothelial growth factor
VRE:	vancomycin-resistant enterococci

PHYSIOLOGIC WOUND HEALING

Normal wound healing requires proper circulation, nutrition, immune status, and avoidance of negative mechanical forces. The process usually takes 3 to 14 days to complete and has three phases: inflammation, proliferation, and remodeling with wound contraction[8-10] (Fig 1). During the inflammatory phase, neutrophils and macrophages appear in the wounded area to phagocytize bacteria and debris. A functioning immune system and adequate supply of growth factors are necessary in this phase of wound healing. In the proliferative phase, fibroblasts produce a collagen matrix, new blood vessels invade the forming granulation tissue, and epidermal cells migrate across the wound surface to close the breach. Protein or vitamin deficiencies may impair
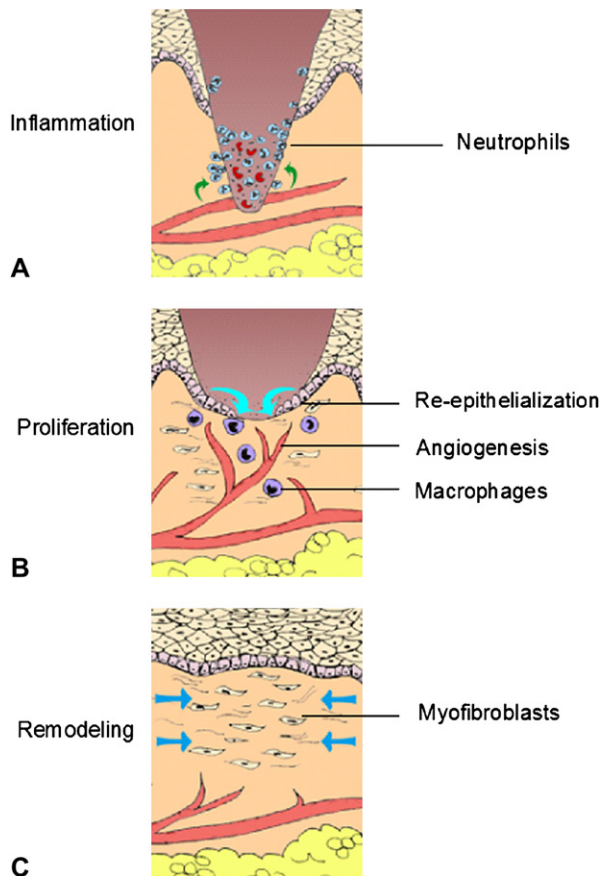
Fig 1. Normal wound healing. Physiologic wound healing occurs in three phases that may overlap in time.[9,10] **A**, Inflammatory phase: aggregated platelets and damaged parenchymal cells at the site of tissue injury secrete growth factors and other chemical mediators of wound healing to attract and activate inflammatory cells and fibroblasts. Vasodilation and increased permeability of local capillaries permit neutrophils to move into the wound site to phagocytize bacteria and debris. **B**, Proliferative phase: within hours of wounding, the process of re-epithelialization begins. Epidermal cells detach from the basement membrane to migrate across the wound surface. Activated macrophages phagocytize debris and release vascular endothelial growth factor (VEGF) and other growth factors to stimulate granulation tissue formation. **C**, Remodeling: fibroblasts remodel the collagen matrix to enhance tissue strength and decrease wound thickness. During the second week of healing, fibroblasts assume a myofibroblast phenotype to facilitate contraction of the forming scar.

collagen production, and necrotic tissue in the wound bed may impede re-epithelialization. During the remodeling phase, fibroblasts reorganize the collagen matrix and ultimately assume a myofibroblast phenotype to effect connective tissue compaction and wound contraction. Wounds gain about 20% of their final strength in the first 3 weeks of

normal wound healing through collagen deposition, remodeling, and wound contraction.[10] When any of the components of the wound healing process is compromised, healing may be delayed.

APPROACH TO THE PATIENT WITH A NONHEALING WOUND

A thorough medical history and physical examination are essential to every patient evaluation. Healthy patients usually heal in a timely manner, while patients with chronic wounds almost always have factors that impair the ability to heal. Thus, the clinician must assess the patient's general health status. History-taking should address:

1. Description of how the wound occurred
2. Past history of wounds, including previous diagnoses and response to treatment
3. Family history of chronic wounds and/or poor healing
4. Dermatologic conditions that predispose to ulceration
5. Edema
6. The presence or absence of pain, with particular emphasis on pain quality, precipitating factors, and methods of ameliorating pain
7. Systemic conditions that may predispose to wound development or poor healing, including HIV/AIDS, sickle cell anemia, Raynaud syndrome, rheumatologic disease, chemotherapy, anemia, weight loss, viral hepatitis, illicit drug use, transfusions, or neurologic disorders, to name the most common
8. Previous hospitalizations and surgeries, including insertion of meshes, prostheses, or other foreign bodies

Medications
All systemic and topical medications used by the patient should be recorded. Antiinflammatory and immunosuppressive medications can compromise wound healing and put patients at increased risk for wound infection.[11,12] Specific inquiries about topical therapies are essential, because a substantial number of patients have contact allergies to preparations containing balsam of Peru, neomycin, bacitracin, and other common ingredients.[13-16] The resultant delayed hypersensitivity reactions can retard healing.[17] Additionally, many commonly used topical antiseptics are directly toxic to human cells.[18-21]

Nutrition
Sound nutritional status is essential for successful wound healing and immune response to injury.[22,23] Carbohydrates and fats supply cellular energy and

protein is utilized in anabolic repair. Sufficient quantities of vitamins A, C, and E, selenium, thiamine, pantothenic acid, zinc, copper, and manganese have been reported to be essential for healing.[24] Frail, elderly, and institutionalized patients are at particularly high risk for malnutrition,[23,24] but even obese patients (especially those who have undergone bariatric surgery) may be malnourished and susceptible to nonhealing wounds.

Social history

It is essential to understand each individual patient's motivations, capabilities, home environment, family support, and financial resources, because each of these factors directly affects wound care. In addition, general habits, such as tobacco and alcohol use, should be noted, because both are associated with compromised wound healing.[25,26] Intravenous drug users are inherently prone to developing wounds and infections related to repetitive trauma with nonsterile instruments, the injection of foreign materials, not to mention HIV and hepatitis C infection. International travel and occupational exposures should also be considered, because these may be directly involved in the etiology of a nonhealing or relapsing wound.

Physical exam

Examination of the extremity. The vast majority of chronic wounds occur on the lower extremity. A thorough limb evaluation may reveal signs of predisposing systemic disease. For example, edema, hemosiderosis, lipodermatosclerosis, and varicosities are markers of venous disease. Duplex ultrasonography can be used to confirm the presence of venous insufficiency. Cool extremities with slow capillary refill and dependent rubor reflect arterial insufficiency. Ankle-to-brachial and toe-to-brachial blood pressure indices (ABI and TBI, respectively) can be used to gauge a limb's arterial supply. Doppler ultrasound can also assist in evaluating arterial supply, showing triphasic waveforms in areas of normal arterial flow, and biphasic or monophasic waveforms when arterial stenosis is present. Patients with compromised lower extremity sensation, as in diabetic neuropathy, are at increased risk for foot wounds. Thus, the Semmes–Weinstein 10-gram monofilament evaluation of lower extremity sensation is an essential component of the physical exam. Finally, the presence of regional adenopathy suggests infection of the extremity.

Ulcer appearance. The ulcer must be cleansed of all slough, eschar, and debris so that its borders, base, and surrounding skin are clearly visible. The wound's edges can provide clues to its etiology.

Sharply demarcated, "punched out" lesions are suggestive of arterial insufficiency (Fig 2, *A*), while poorly defined, irregular borders suggest venous ulceration (Fig 2, *B*). Firm, rolled edges should raise suspicion for neoplasic involvement (Fig 3, *A*), and undermined borders are characteristic of pyoderma gangrenosum and Behçet's disease. Geometric or linear wounds may suggest trauma or factitial processes.

At each encounter, the clinician should record the color and texture of the ulcer base. Healthy granulation tissue is pink and plump in appearance, whereas purple, gelatinous, purulent, or bloody tissue may indicate infection (Fig 3, *B* and *C*). The appearance and quantity of wound exudate should be noted as well, because this directly affects dressing selection and wound care.

Measurements. The wound dimensions must be measured at each visit to track healing over time. Dimensions of greatest length, greatest perpendicular width, and greatest depth should be recorded. Additionally, the clinician must document the extent to which wound edges are undermined and the presence of sinuses or tunnels. If bone is directly visualized at the wound base or can be felt by probing with a blunt instrument, an evaluation for osteomyelitis is appropriate. Radiologic assessments, including plain films, magnetic resonance imaging (MRI), computed tomography (CT) scans (when metal prostheses have been placed), and indium-111 leukocyte scans may be useful.

Laboratory evaluations

General laboratory values can provide important insights into a patient's general health and ability to heal. Anemia or infection, as indicated by abnormalities in the complete blood count, and protein malnutrition, reflected in the serum albumin and prealbumin levels, can impair wound healing. Elevations of the erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP) may indicate ongoing infection or inflammation. The hemoglobin A1c level provides a measure of a diabetic's blood sugar control over the preceding months. In patients for whom there is a suspicion of underlying vasculitis, hyperviscosity, or thrombosis, laboratory investigations for specific rheumatologic, infectious, or hematologic processes may be instructive. Levels of antithrombin III, factor V Leiden, and proteins C and S, as well as coagulation times, can point to prothrombotic conditions. Family history and early age of ulcer onset may render testing for sickle cell anemia appropriate. Markers of autoimmunity may suggest rheumatologic diseases, and cryoglobulins

Fig 2. Common chronic wounds. **A**, Arterial ulcer at the lateral malleolus. This ulcer has sharp margins and a punched out appearance. The surrounding skin is dry, shiny, and hairless. This wound was treated with a sheet hydrogel dressing to hydrate the area and provide pain relief. **B**, Venous stasis ulcer with irregular border, shallow base, and surrounding hemosiderosis and lipodermatosclerosis. This wound was treated with an absorptive hydrofiber dressing and Unna boot. **C**, Diabetic foot ulcer with surrounding callus. Severe diabetic neuropathy and bony deformity contributed to wound formation. Sharp debridement was employed to remove the surrounding callus, and an alginate dressing was then used to manage the high level of drainage. The patient was later fitted with appropriate offloading shoes. **D**, Pressure ulcer in a paraplegic patient, causing full-thickness skin loss. Because the wound edges had rolled and become quiescent, the patient was taken to the operating room for wound edge debridement. A topical negative pressure (or vacuum-assisted closure) dressing was subsequently applied, and the patient received an offloading home mattress.

and dysproteinemias may indicate hepatitis C or underlying neoplasms.

Wound cultures are necessary in instances where there is suspicion of infection. To avoid misinterpreting positive cultures from superficial wound colonization, deeper tissue should be sampled and specimens sent for quantification of colony count per gram of tissue. Tissue can also be submitted for histologic examination and stained for bacteria, mycobacteria, and fungi.

COMMON CHRONIC WOUNDS
Venous ulcers

Venous stasis ulcers account for more than half of all lower extremity chronic wounds.[27] Approximately 1% to 2% of the adult population has a history of active or healed venous ulceration.[4,5] It is not unusual for this type of wound to persist for 5 years or longer.[6] Venous stasis ulcers are more common in women than men and increase in incidence with age.[4]

Fig 3. Wound complications. **A**, Marjolin's ulcer in a nonhealing pressure sore. Marjolin's ulcer is a squamous cell carcinoma that can develop in a longstanding scar or chronic wound. A nonhealing wound with firm, rolled borders warrants biopsy evaluation. **B**, Infection. The exudate overlying an infected wound may be malodorous, with a green or blue hue. This wound requires debridement. **C**, Infection. Dark red granulation tissue that bleeds easily on contact may be a sign of infection. **D**, Maceration. The periwound area here is white, plump, and friable. A highly absorptive dressing such as an alginate or hydrofiber, used in combination with a periwound protectant (for example, a drying calamine/zinc oxide paste), would be an appropriate choice for this wound. **E**, Eschar. Heel eschar in a patient with peripheral vascular disease should not be debrided. **F**, Dry wound. This desiccated wound was debrided and treated with a moisture-donating hydrogel dressing. **G**, Skin tear. Patients with thin, fragile skin are susceptible to skin tears as a result of certain strongly adherent dressings. A nonadhesive wrapped dressing would be preferable in this patient.

Venous ulcers usually occur in the setting of longstanding venous hypertension and insufficiency, and are a consequence of venous thrombosis and/or reflux through incompetent valves. Patients with chronic venous insufficiency commonly complain of swelling and aching of the legs that is worse at the end of the day and improves with leg elevation. These wounds can occur anywhere there is reflux between the deep and superficial venous systems. The medial malleolus is the most common site.[28]

The borders of venous ulcers are typically irregular and ill defined, and the wound bed is usually shallow (Fig 2, *B*). Chronic wounds caused by sickle cell anemia or other procoagulant disorders may have a similar appearance. Venous ulcers tend to be larger than most other chronic wounds, often involving the lower extremity circumferentially. The surrounding skin may exhibit pitting edema, induration, hemosiderosis, varicosities, lipodermatosclerosis, atrophie blanche, and/or stasis dermatitis.

Arterial ulcers

Arterial leg ulcers are a consequence of inadequate blood supply to the skin. Atherosclerotic disease is the most common cause,[29] although thromboembolic disease can also infarct skin and lead to ulcer formation. The risk for lower extremity arterial ulceration is increased in smokers, diabetics, elderly patients, and individuals with evidence of arterial disease at other sites.[30,31] Arterial insufficiency often causes symptoms of intermittent

claudication and rest pain (relieved by hanging the legs in the dependent position). Cool feet, weak pedal pulses, and slow toe capillary refill on physical examination support the diagnosis of arterial insufficiency. Doppler ultrasound assessment of the distal pulses, ABIs, and TBIs can confirm a compromised limb arterial supply.

Arterial ulcers are usually round with a sharply demarcated border. These wounds typically occur distally, often over bony prominences[29,30] (Fig 2, *A*). The surrounding skin may be hairless, shiny, and atrophic. Wound pain is often significant and is exacerbated by leg elevation. Arterial leg ulcers may benefit from surgical correction of the underlying vascular problem and restoration of the peripheral blood flow.[29] Arterial disease can be found in approximately 25% of patients with leg ulcers. Ulceration of mixed arterial and venous etiology is not uncommon.[30,32]

Diabetic foot ulcers

Diabetics have a 15% to 25% lifetime risk of developing a foot ulcer, usually as a consequence of diabetes-associated peripheral neuropathy or vascular disease.[33,34] Peripheral motor neuropathy weakens the intrinsic muscles of the feet, producing structural deformities that, when coupled with sensory neuropathy, increase the risk for wounds from continuous mechanical stress.[34] Typically, a thickened callus forms at the area of repeated pressure and ultimately breaks down, leading to ulcer formation[31] (Fig 2, *C*). The insensate foot is also at increased risk for wounds from acute trauma.

Diabetic foot ulcers are often nonhealing because of poor blood sugar control, poor tissue oxygenation, and impaired immune response to injury.[35] Depressed immune system functioning also puts diabetics at increased risk for wound infection.[36-38] Diabetic foot ulcers are a major risk factor for limb amputation,[39] because osteomyelitis of the underlying bone is not uncommon.[40] For healing and avoidance of recurrence, patients with sensory neuropathy must wear protective footwear at all times to prevent repeated trauma. Many patients also require custom offloading shoes to redistribute weight off of the ulcer site.

Pressure ulcers

Pressure ulcers are caused by impaired blood supply and tissue malnutrition as a result of prolonged pressure, friction, or shear. Tissue compression exceeding the capillary filling pressure of 32 mm Hg that lasts longer than 2 hours can cause local ischemia and necrosis. Skin overlying bony prominences (eg, sacrum, malleoli, or hips) is especially vulnerable.[41]

Pressure ulcer development begins with non-blanching erythema of intact skin and can progress to full-thickness skin loss with extensive destruction of underlying tissue (Fig 2, *D*). Individuals who are immobile, paralyzed, elderly, or malnourished are at highest risk.[23,41] Frequent repositioning and off-loading with special beds and cushions are key components of pressure ulcer prevention and management.

Vasculitis

Immune complex deposition in vessel walls can lead to inflammation and vessel necrosis. Palpable purpura is a common early cutaneous manifestation from which ulceration may eventually ensue (particularly if medium-sized vessels are involved). Lesions tend to occur over dependent areas and may be very painful. Vasculitis may be associated with autoimmune, infectious, medication-related, malignancy-related, or idiopathic etiologies. Systemic symptoms may accompany the cutaneous manifestations and can help to define the underlying etiology.[42]

Pyoderma gangrenosum

Pyoderma gangrenosum (PG) is a noninfectious neutrophilic dermatosis that causes recurrent painful inflammatory ulcerations. PG is associated with underlying systemic disease, such as inflammatory bowel disease, rheumatoid arthritis, or malignancy in up to 70% of cases.[43-47] Lesions begin as tender pustules with an inflammatory periphery that expand to form sharply circumscribed ulcers with violaceous, undermined borders. PG commonly has a pretibial location, but can occur anywhere. The pathogenesis is poorly understood and diagnosis is generally made on clinical grounds. Ulcer severity may parallel that of the underlying disease, and treatment of the systemic condition often leads to improvement of the skin.[44-46]

PRINCIPLES OF WOUND CARE
Moisture and occlusion

The Greek physician Galen of Pergamum (120-201 A.D.) noted empirically that wounds heal optimally in a moist environment.[48] Nevertheless, for nearly 2000 years, therapeutic efforts focused on drying the wound site, with absorptive gauzes a mainstay of wound management.[49] It was not until the 1960s that Winter proved the critical role of moisture in healing, when he demonstrated that acute wounds covered with moisture-retentive occlusive dressings healed twice as rapidly as similar wounds left exposed to air.[50] In contrast, excessively

dry wound healing environments actually caused further tissue death.[51]

In the latter half of the 20th century, as clinical data accumulated in support of moist wound healing, manufacturers began producing polymer-based occlusive wound dressings designed to preserve and protect a moist wound environment.[48,49] Modern occlusive wound dressings may be either fully occlusive (impermeable to fluids and gases) or semiocclusive (impermeable to fluids and partially permeable to gases like oxygen and water vapor).[52] Not only do these dressings speed re-epithelialization; they also stimulate collagen synthesis and create a hypoxic environment at the wound bed that promotes angiogenesis.[53-55] An added benefit of moisture-retentive dressings is that many patients experience pain relief with their use.[56-59]

Despite initial fears that occlusive dressings would promote wound infection, it has now been shown that they actually decrease infection rates compared to nonocclusive dressings.[60] This difference is likely attributable to occlusive dressings' ability to maintain a more effective barrier against external contamination.[61,62] Additionally, some occlusive dressings decrease the pH at the wound surface, helping to create an environment inhospitable to microbial growth.[54]

While moisture is essential for proper healing, excessive wetness on the wound bed can be problematic. Occlusive dressings applied to highly exudative wounds may cause maceration of the surrounding skin. Overhydrated, macerated tissue is soft, white, and friable (Fig 3, D) with a tendency to break down, which can delay wound healing or make the wound deteriorate further.[13,63] Furthermore, the fluid from chronic wounds may actively interfere with the healing process. Chronic wound fluid inhibits fibroblast proliferation[64,65] and contains proteases that destroy extracellular matrix material and growth factors.[66-68] The ideal wound dressing should thus absorb exudate without excessively drying the wound.

Bacterial colonization versus infection

Bacteria are present on virtually all open wounds. When growth and death of microbes are kept in balance by host defenses, a wound is considered to be colonized.[69] In some instances, colonization may actually hasten wound healing by increasing wound bed perfusion.[70,71] At the point of critical colonization, however, host defenses can no longer maintain this balance and the wound may enter a nonhealing, chronic inflammatory state.[69] Bacterial loads in excess of 10^5 organisms per gram of tissue are said to impede wound healing, though the status of the host immune system and the number and types of

bacterial species present may alter this threshold.[69,72-74] Wounds become clinically infected when host defenses are overwhelmed.[69] Infected wounds often demonstrate increased erythema, edema, warmth, pain, and exudate (Fig 3, B and C). There may be associated malodor as well. Systemic signs, such as fever, chills, and leukocytosis, suggest that the infection may have progressed to bacteremia or septicemia.

Infections of chronic wounds are often polymicrobial, with *Staphylococcus aureus* and anaerobes among the most common pathogens.[74,75] Whenever possible, clinically infected wounds should be cultured and microorganism sensitivities determined before systemic antimicrobial agents are prescribed. Signs of wound infection are sometimes subtle, especially in the elderly, who may lack brisk inflammatory responses. Mycobacterial and fungal infections may similarly lack intense signs of inflammation. A high index of suspicion is warranted for wounds with inexplicable failure to heal.

Debridement

Debridement is the process of removing slough, eschar, exudate, bacterial biofilms, and callus from the wound bed in order to permit healing. Sharp debridement using a scalpel, forceps, scissors, and/or curette is the most rapid and precise method, though the procedure may be painful even when local anesthetics are used. In sharp debridement, nonviable tissue and debris are removed until normal, well vascularized tissue appears. This has the benefit of converting chronic wounds into acute wounds with improved ulcer bed perfusion and an acute wound healing response. Neutrophils and macrophages recruited to the area can then secrete growth factors and phagocytize bacteria and nonviable tissue.[76,77] Sharp debridement can be used on diabetic foot ulcers, venous leg ulcers, and pressure ulcers, but caution should be exercised with arterial ulcers because ischemic tissues tend to desiccate after debridement, potentially causing ulcer enlargement.[29,76-78] In particular, eschar overlying heel wounds in patients with suspected lower extremity vascular compromise should generally be left in place (Fig 3, E). Still, for appropriate patients, sharp debridement is our preferred debridement approach. Second-line alternative techniques are described below.

Wet-to-dry debridement involves placing saline-moistened gauze over the wound, allowing the gauze to dry out, and then removing the dry gauze with nonviable tissue adhered. The value of wet-to-dry debridement is often questioned because this technique is associated with a high degree of pain

Table I. Summary of basic wound dressings[94,195]

Product	Advantages	Disadvantages	Indications	Comment
Gauzes	Inexpensive Accessible	Drying Poor barrier	Packing deep wounds	Change every 12-24 hours
Films	Moisture-retentive Transparent Semiocclusive Protects wound from contamination	No absorption Fluid trapping Skin stripping	Wounds with minimal exudate Secondary dressing	Can leave in place up to 7 days or until fluid leaks
Hydrogels	Moisture-retentive Nontraumatic removal Pain relief	May overhydrate	Dry wounds Painful wounds	Change every 1-3 days
Hydrocolloids	Long wear-time Absorbent Occlusive Protects wound from contamination	Opaque Fluid trapping Skin stripping Malodorous discharge	Wounds with light to moderate exudate	Can leave in place up to 7 days or until fluid leaks
Alginates and hydrofibers	Highly absorbent Hemostatic	Fibrous debris Lateral wicking (alginates only)	Wounds with moderate to heavy exudate Mild hemostasis	Can leave in place until soaked with exudate
Foams	Absorbent Thermal insulation Occlusive	Opaque Malodorous discharge	Wounds with light to moderate exudate	Change every 3 days

and has only limited selectivity for nonviable tissue. That is, there is a tendency to strip the wound of valuable fibroblasts, macrophages, and keratinocytes along with slough and debris.[79]

Autolytic debridement is the gentle separation of slough and necrotic tissue from the wound bed that occurs slowly in a moist wound environment. Moisture-donating wound dressings promote autolytic debridement by rehydrating desiccated and devitalized tissue, aiding its separation from healthy tissue. Autolytic debridement may take several weeks, but can be useful for instances where sharp debridement is inappropriate (eg, in patients with bleeding tendencies).

Enzymatic debridement via topical protease preparations may also be employed. These ointments contain enzymes that target the fibrin and collagen of necrotic tissue and wound exudate. Papain—urea preparations (eg, Accuzyme; Healthpoint, Ltd, Fort Worth, TX), for example, contain papain, a nonspecific cysteine protease derived from the Carica papaya, and urea, a protein denaturant.[80] Collagenase preparations (eg, Santyl; Healthpoint, Ltd), on the other hand, are derived from *Clostridium histolyticum* and target collagen specifically.[81] Small clinical- and laboratory-based investigations suggest that papain—urea may provide somewhat more extensive debridement than collagenase.[82-84] Like autolytic debridement, enzymatic debridement can take weeks to achieve the desired effects.[85] Some patients experience a temporary burning sensation or erythema with application; thus, care should be taken to ensure that the product contacts only the nonviable tissue within the wound and not the surrounding skin. To increase topical enzyme penetration of tough eschar, cross-hatching by sharp incision before application can be beneficial.

WOUND DRESSINGS
Past to present

Translations of the ancient Egyptian Ebers Papyrus (1550 B.C.) reveal descriptions of wound dressings composed of lint (vegetable fibers), grease (animal fats), and honey. Modern day scholars believe that the lint may have been used for its absorbency, the grease for its barrier properties, and the honey for its antibacterial effects.[48] Thus, even the earliest wound dressings appear to have been designed to manipulate the wound environment in purposeful ways. This same approach is utilized in the development of modern wound dressings.

The enormous array of wound care products on the market today (Table I) makes selection of the most appropriate dressing for a given wound a sometimes daunting task. The current concept of the "ideal wound dressing" is one that removes

Table II. Barrier products

Product	Company	Cost/wk*	Comment
Vaseline petroleum jelly	Kendall	$0.60	Protects periwound[162]
			Can interfere with dressing adherence[13]
Zinc oxide paste	Generic	$4.37	Protects periwound[162]
			Antiinflammatory, may improve healing[160-162]
			Can interfere with dressing adherence[13]
Calmoseptine ointment	Carrington	$6.34	Protects periwound
			Helps to dry out macerated tissue
			Contains calamine, zinc oxide, menthol, lanolin
			Helps relieve discomfort, itching
Cavilon No Sting Barrier Film	3M	$11.95	Protects periwound
			Single-use wand
			Easier removal than zinc oxide[196]
All Kare Barrier Wipes	ConvaTec	$2.49	Protects periwound
			Single-use wipes

*Assumes a daily re-application of 0.25 oz. or daily use of single-use products. This table is not meant to endorse a single product and should not be considered inclusive. Costs are based on prices listed in the Edgepark Surgical 2005 ordering catalog[197] or at www.drugstore.com.[198]

Table III. Gauzes

Product	Company	Cost/wk*	Comment
Curity gauze sponge	Kendall	$1.02	100% cotton sterile gauze
Curity packing strip	Kendall	$3.08	½″ width 100% cotton gauze ribbon
Vaseline gauze	Kendall	$5.95	Gauze impregnated with petrolatum
			Less adherent than plain gauze
Xeroform	Kendall	$25.90	Gauze impregnated with 3% bismuth tribromophenate (xeroform, an antiseptic and deodorizer) in petrolatum
			Less adherent than plain gauze
Mesalt	Mölnlycke	$20.25	Hypertonic sodium chloride-impregnated gauze
			Highly absorbent
			Discourages bacterial growth
			Inhibits overexuberant granulation tissue formation
Iodoform impregnated packing strips	Derma Sciences/ Dumex Medical	$2.73	½″ width iodoform (antiseptic) impregnated gauze ribbon

*Approximate cost per week to treat a 2 in × 2 in wound or 2-in deep sinus wound (for ribbon dressing) with daily dressing changes. This table is not meant to endorse a single product and should not be considered inclusive. Costs are based on prices listed in the Edgepark Surgical 2005 ordering catalog.[197]

excess exudate, maintains a moist environment, protects against contaminants, causes no trauma on removal, leaves no debris in the wound bed, relieves pain, provides thermal insulation, and induces no allergic reactions.[86,87] Given the biologic complexity of chronic wounds, it is unlikely that there will ever be a single dressing that is perfect for every wound type.

The ideal wound dressing should also be cost effective.[86,87] In Tables II through X, we list representative products of each dressing type. To facilitate product cost comparisons, we have included approximations of "cost per week" to treat a standard sized wound, taking into consideration the average frequency of application. (These cost values do not reflect the true relative cost efficacies of these products, however, which would also take into consideration differences in healing time and variations in required nursing time associated with each dressing type.)

Periwound protection

Wound-associated inflammation can compromise the barrier integrity of the surrounding skin, rendering it especially vulnerable to damage from excess moisture, wound fluid proteases, and dressing adhesives.[88-90] This area is also at increased risk for contact dermatitis from topical agents.[91] Barrier creams, ointments, and other periwound protectants (Table II) are available to protect the skin around the ulcer. We use these preparations frequently.

Table IV. Films

Product	Company	Cost/wk*	Comment
Bioclusive	Johnson & Johnson	$6.51	Classic film dressing
Blisterfilm	Kendall	$6.10	Adhesive-free wound contact area
OpSite Flexigrid	Smith & Nephew	$6.40	Printed with wound measurement grid to track healing
Tegaderm HP	3M	$7.98	Extra-strength adhesive for wounds with moderate moisture

*Approximate cost per week to treat a 2 in × 2 in wound with dressing changes every 3 days. This table is not meant to endorse a single product and should not be considered inclusive. Costs are based on prices listed in the Edgepark Surgical 2005 ordering catalog.[197]

Table V. Hydrogels and related products

Product	Company	Cost/wk*	Comment
Restore hydrogel	Hollister	$15.05	Amorphous gel
Carrasyn hydrogel	Carrington	$15.40	Amorphous gel
			Contains aloe vera gel extract
SAF-Gel	ConvaTec	$16.43	Contains alginate for increased absorption
Curagel	Kendall	$12.90	Sheet hydrogel
			Superior pain control
XCell cellulose dressing	Xylos	$36.43	Sheet of biosynthesized cellulose from *Acetobacter xylinum* bacteria
			Can absorb or donate moisture depending on wound microenvironment[199]

*Approximate cost per week to treat a 2 in × 2 in wound with 0.25 oz. amorphous gel application daily or sheet dressing application every 3 days (longer average wear-time). This table is not meant to endorse a single product and should not be considered inclusive. Costs are based on prices listed in the Edgepark Surgical 2005 ordering catalog.[197]

Gauzes

Plain dry gauze has historically been one of the most popular wound dressings. While plain cotton gauze does offer good absorption, it also promotes desiccation of the wound base, which can be detrimental to healing.[51] Furthermore, dry gauzes often bind to the wound surface, causing pain and trauma to the wound bed at dressing changes. Finally, because gauze dressings are susceptible to full-thickness saturation with wound fluid ("strike-through"), they have limited ability to provide an effective barrier against bacterial invasion.[62]

Although many knowledgeable clinicians insist that wet-to-dry gauze dressings are as effective as the newer, more expensive, moisture controlling dressings, a recently published study of 767 wounds treated using standardized dressing protocols found that moisture-retentive dressings are associated with faster healing times than gauze dressings.[92] Furthermore, although they are more expensive per individual dressing, moisture-retentive dressings are more cost effective over time as well.[92]

Many modern gauzes are impregnated with substances intended to optimize the healing environment (Table III). For example, petrolatum-impregnated gauze is less drying and less adherent than dry gauze, but it also offers less absorbency.[87]

Sodium chloride—impregnated gauze, on the other hand, has the benefits of absorbing well, creating a hypertonic environment that is hostile to bacteria, and preventing formation of excess granulation tissue, but it has a tendency to adhere to and/or desiccate the wound surface. (We often use pre-moistened sodium chloride gauze to dress very wet wounds requiring an absorptive dressing.)

Gauze dressings are available in both pad and ribbon form. Gauze ribbons are ideal for treating deep wounds and sinus tracts, which must heal from the base upwards in order to eliminate dead space and prevent abscess formation. Loose packing with gauze ribbons encourages healing from the base outward. Packing should never be tight, because this may cause localized ischemia and wound enlargement.[93]

Films

Films are transparent, conformable, adhesive dressings (Table IV) that may be used as primary dressings directly over a wound or as secondary dressings to secure various nonadhesive primary dressings in place. These thin membranes are semi-occlusive, permitting the exchange of oxygen and water vapor between the wound bed and the environment while remaining impermeable to liquid and

Table VI. Hydrocolloids

Product	Company	Cost/wk*	Comment
Tegasorb	3M	$13.06	Becomes transparent with use[110] Film backing
DuoDERM CGF	ConvaTec	$17.00	Prevents lateral invasion of microorganisms from the dressing edge[61] Foam backing
Comfeel Plus	Coloplast	$19.16	Contains alginate for increased absorption Film backing

*Approximate cost per week to treat a 2 in × 2 in wound with dressing changes every 4 days. This table is not meant to endorse a single product and should not be considered inclusive. Costs are based on prices listed in the Edgepark Surgical 2005 ordering catalog.[197]

Table VII. Alginates and related products

Product	Company	Cost/wk*	Comment
Kaltostat	ConvaTec	$14.61	High guluronic acid content
Sorbsan	Bertek	$12.15	High mannuronic acid content Tendency for lateral wicking[118]
Tegagen	3M	$9.71	Available in high integrity (HI) and high gelling (HG) formulations
AlgiSite	Smith & Nephew	$11.12	High mannuronic acid content
Aquacel Hydrofiber	ConvaTec	$15.81	Hydrofiber dressing composed of sodium carboxymethylcellulose (CMC) fibers More absorptive than alginates[200] Vertically wicks to prevent periwound maceration[201]

*Approximate cost per week to treat a 2 in × 2 in wound with dressing changes every 3 days. This table is not meant to endorse a single product and should not be considered inclusive. Costs are based on prices listed in the Edgepark Surgical 2005 ordering catalog.[197]

bacterial contaminants. Film dressings are not absorbent; they manage moisture by vapor transmission only.[49] For this reason, films should be reserved for wounds with minimal exudate. If used inappropriately over a wound with heavy exudate, films can cause fluid trapping and maceration.[94]

Because films are transparent, wounds can be visualized without having to remove the dressing. Therefore, dressing changes may be made as needed, rather than on a rigid schedule.[95] The acrylic adhesive on most film dressings is deactivated by moisture, so that films adhere to the dry periwound area only. This property minimizes wound bed trauma at dressing changes.[96] Still, there may be a tendency to strip delicate new epidermis from newly re-epithelialized areas of a healing wound if films are applied and removed too frequently.[53]

Hydrogels

Hydrogels are water-based products used to maintain a moist wound-healing environment (Table V). They are best suited for dry wounds or wounds with low levels of exudate, and should be avoided in wounds with heavy exudate because the excess moisture can lead to maceration of periwound skin.[95,97] Hydrogels also promote autolytic debridement of slough and necrotic tissue, making

them suitable debriding agents in patients for whom sharp debridement is contraindicated.[97,98] A key advantage of hydrogels is that they can be applied and removed with minimal pain or trauma to the wound bed. Additionally, many patients experience pain relief with hydrogel dressings, likely because of their cooling effects.[99-101] Hydrogels are available in amorphous gel and sheet form; in our experience, pain relief is most pronounced with sheet hydrogels.

While laboratory-based studies have noted differences in the fluid-handling capabilities of different hydrogels,[102,103] clinical evidence suggests that no single hydrogel is more or less efficacious than others in practice.[101,104] Several small studies have shown hydrogels to perform similarly to moist gauze and hydrocolloid dressings in rate of pressure ulcer healing.[105-107]

Hydrocolloids

In contrast to the fluid-donating hydrogels, hydrocolloids (Table VI) provide absorption. These adhesive, occlusive, conformable dressings absorb wound exudate to form a hydrophilic gel that helps to maintain a moist healing environment.[108] Compared to films, hydrocolloids have less moisture vapor transmission; thus they rely predominantly on absorption for exudate management.[108] Hydrocolloids

Table VIII. Foam dressings

Product	Company	Cost/wk*	Comment
3M Adhesive Foam	3M	$14.64	Border of transparent adhesive film
Lyofoam C	ConvaTec	$24.17	Contains activated carbon for odor control
Allevyn hydrocellular dressing	Smith & Nephew	$15.79	Trilaminate structure with nonadherent wound contact layer, absorbent central layer, and semipermeable film outer layer
Allevyn cavity dressing	Smith & Nephew	$55.26	Cavity dressing Absorbent foam chips covered with a nonadherent wound contact layer

*Approximate cost per week to treat a 2 in × 2 in surface wound with a sheet foam or 2-in diameter cavity wound with a cavity dressing, with dressing changes every 3 days. This table is not meant to endorse a single product and should not be considered inclusive. Costs are based on prices listed in the Edgepark Surgical 2005 ordering catalog.[197]

Table IX. Antimicrobial dressings

Product	Company	Cost/wk*	Comment
Iodosorb gel (cadexomer iodine)	Healthpoint	$28.76	Cadexomer iodine plus compression gives superior venous ulcer healing than moist gauze plus compression[202,203] May speed pressure ulcer healing[204]
Silver sulfadiazine 1% cream	Generic	$5.11	Contains silver ions and sulfonamide Cream may form pseudoeschar as it dehydrates; must be removed prior to reapplication Proinflammatory[205] Tendency to cause temporary local discoloration[150,151] Avoid in sulfur-sensitive individuals[137]
Aquacel Ag Hydrofiber	ConvaTec	$32.39	Silver-impregnated hydrofiber dressing
Acticoat 7	Smith & Nephew	$23.92	Coated with nanocrystalline silver Rapid release of silver ions[144,148]
Contreet Foam	Coloplast	$15.86	Foam dressing Rapid release of silver ions[148,206]
Actisorb Silver 220	Johnson & Johnson	$18.19	Contains activated carbon (odor fighting) and metallic silver Relatively low silver content Sequesters and inactivates microorganisms within the dressing[148]
Silverlon Wound Contact Dressing	Argentum	$16.38	Silver-coated wound contact layer, absorbent pad, and film backing Limited activity against *S aureus* despite high silver content[149]
SilvaSorb	Medline	$53.61	Silver-containing hydrogel
SilverCel	Johnson & Johnson	$17.72	Pad composed of alginate, hydrofiber, and silver-coated nylon fibers

*Approximate cost per week to treat a 2 in × 2 in wound. This table is not meant to endorse a single product and should not be considered inclusive. Costs are based on prices listed in the Edgepark Surgical 2005 ordering catalog[197] or at www.drugstore.com.[198]

are best used over wounds with low to moderate amounts of exudate.[80] They are less appropriate for wounds with large amounts of exudate because of the risk of periwound maceration and because the high degree of moisture can cause the dressing to separate from the wound bed.[103,109]

An important advantage of hydrocolloid dressings is their relatively long wear-time (Table I), a feature that decreases the cost, inconvenience, and local

trauma associated with dressing changes.[2,110] Additionally, hydrocolloid dressings can protect against shear force at the skin surface, which is a contributor to pressure ulcer development.[109] Certain precautions must be taken with hydrocolloid dressings. Although the hydrocolloid adhesive is inactivated by moisture,[49] it may adhere aggressively to the dry periwound area, potentially causing injury at dressing changes. Barrier products and periwound

Table X. Compression systems

Product	Company	Cost/wk*	Comment
Unna boot	Generic	$23.00	Moist zinc oxide gauze covered with elastic compression bandage (Fig 4)
			Change every 7-10 days
DYNA-FLEX Compression System	Johnson & Johnson	$37.44	3-layer system
			Change every 7 days
			Imprinted graphic to ensure appropriate degree of compression
Profore Bandaging System	Smith & Nephew	$34.20	4-layer system
			Change every 7 days

*Assumes weekly reapplication. This table is not meant to endorse a single product and should not be considered inclusive. Costs are based on prices listed in the Edgepark Surgical 2005 ordering catalog.[197]

protectants can be employed to minimize this type of damage. Another downside of treatment with hydrocolloid dressings is their tendency to produce a brown, often malodorous exudate that can be mistaken for infection and can be troubling for the patient.[94]

A meta-analysis of 12 randomized controlled trials comparing hydrocolloid dressings to conventional gauze dressings for the treatment of chronic wounds found that hydrocolloids improved the rate of ulcer healing.[2] This benefit appears most pronounced for pressure sore healing.[111,112] The few trials comparing the efficacy of different hydrocolloid products have found no significant performance differences.[110,111]

Alginates

Alginates are highly absorbent, fibrous dressings (Table VII) that can hold up to 20 times their weight in fluid.[95] Alginate dressings are utilized mainly for their strong absorptive capacity on wounds with moderate to heavy levels of exudate.[113,114] Derived from brown seaweed, alginates contain the calcium and sodium salts of alginic acid, a polymer of mannuronic and guluronic acids. When placed over a moist wound, an ion exchange reaction occurs between calcium in the alginate and sodium in the wound fluid, producing soluble calcium−sodium alginate and forming a gelatinous mass.[94] The resultant gel helps to maintain a moist healing environment.

Because alginates require moisture to function, they are not indicated for dry wounds or wounds covered with hard necrotic tissue unless they are first moistened with saline.[94] It is important that these very absorptive dressings be kept from desiccating over the wound, because the resultant dry environment could delay wound healing.[115] A unique advantage of alginate dressings is that they are inherently hemostatic[116,117] and can be used to control minor bleeding.

Alginates are available as ropes (twisted fibers) or pads (fibrous mats). These dressings are nonadhesive and thus require a secondary dressing to secure them in place. Mannuronic and guluronic acid are present in varying proportions in different alginate products, altering gelling characteristics. Dressings with high concentrations of mannuronic acid form soft amorphous gels that partially dissolve when in contact with wound exudate, whereas high guluronic acid dressings swell in the presence of exudate but retain their basic structure.[113] Depending on its viscosity, the gel that forms when alginates absorb moisture can be removed intact or irrigated away with saline solution during dressing changes.

Several concerns have been raised regarding the use of alginate dressings. Because of a tendency to absorb fluid across the entire surface of the dressing (lateral wicking),[118] some alginates may cause peri-wound maceration if they overlap normal skin. Alginates, therefore, should be cut to the shape of the wound bed. These products also may leave fibrous debris in the wound.[115,119,120] Despite claims that these fibers are readily biodegraded, there have been reports of long-term foreign body−type reactions.[117,119] Furthermore, in vitro studies have raised concerns that alginate dressings may be inhibitory or even cytotoxic to keratinocytes.[121-123] It is unclear how these findings translate clinically, because some studies have reported that alginate dressings accelerate wound healing as compared to control dressings (eg, nonadherent gauze, dextranomer paste) and others have detected no difference in healing rates.[124-126] Comparisons amongst different alginate products demonstrate no significant wound healing performance differences.[118,127]

Foams

Foams are moderately absorbent, semiocclusive dressings that may be used over light to moderately draining wounds (Table VIII). These dressings

provide thermal insulation[114] and protect against shear,[109] while the nonadhesive wound contact layer allows for nontraumatic dressing changes. Foam dressings may occasionally be used for their cushioning effect, though they are not intended as a substitute for proper pressure-relieving devices.[128] Foam sheets are available in a variety of shapes and sizes, with and without adhesive borders. The fluid absorption capacity varies with foam thickness.[57] Some foams have a film backing to prevent exudate leakage and to provide an additional barrier to bacterial contamination.

In studies, foam dressings are comparable to hydrocolloids in terms of ulcer healing.[111] Like hydrocolloids, foams may promote development of excessive malodorous drainage necessitating frequent dressing changes.[129]

Collagens

Recalcitrant chronic wounds are sometimes treated with collagen products, which are thought to support wound healing by laying down a matrix that favors the deposition of new tissue and attracts cell types necessary for healing. Available in particle and sheet form from human, porcine, and bovine sources, most collagen products absorb wound exudate to form a soft biodegradable gel over the wound surface that helps to maintain wound moisture.[80] For example, Promogran (Johnson & Johnson, New Brunswick, NJ) is a freeze-dried matrix of type I bovine collagen and oxidized regenerated cellulose that has been shown in clinical trials to improve the rate of pressure sore and venous ulcer healing.[130,131] Promogran's efficacy may be partly attributable to its demonstrated ability to deplete and/or inactivate factors detrimental to the healing process, such as proteases and free radicals.[132-134] Oasis Wound Matrix (Healthpoint Ltd) is an extracellular matrix sheet dressing derived from porcine small intestinal submucosa that, when used in combination with compression dressings, speeds the healing of venous ulcers as compared to compression dressings alone. Additionally, Oasis reduces venous ulcer recurrence.[135] Finally, Cymetra (Lifecell; Branchburg, NJ) is micronized, decellularized cadaveric dermal matrix, initially developed for cosmetic applications, that has been shown in a series of cases to successfully close recalcitrant sinus tracts.[136]

Antimicrobials

Even in the absence of frank clinical infection, wound healing may be impaired when bacterial colonization counts exceed 10^5 organisms per gram of tissue.[72] Systemic antibiotics should be reserved for clinically infected ulcers,[137,138] but topical antiseptics and antibiotics (Table IX) can be employed to reduce the wound bioburden. Antiseptics are chemical agents that are broadly toxic to microbes, whereas antibiotics are narrow-spectrum antimicrobial agents with specific intracellular targets. In general, microbial resistance is more likely to develop against an antibiotic, whereas antiseptics are more frequently toxic to human tissues.

Topical antibiotics can be very effective when used against sensitive organisms. Mupirocin ointment is particularly effective against Gram-positive organisms, including methicillin-resistant *Staphylococcus aureus* (MRSA), while topical metronidazole gives good anaerobic coverage.[137] Even though they are effective, the topical antimicrobials neomycin and bacitracin are typically avoided in chronic wound care because of their significant potential to induce contact sensitivity.[15-17] Signs and symptoms of contact dermatitis include increased erythema, edema, and pruritus in the distribution of the topical exposure.

Commonly used topical antiseptics include hydrogen peroxide, iodine-based preparations, Dakin's solution (dilute hypochlorite), and silver-releasing agents. Both hydrogen peroxide and povidone–iodine are toxic to human tissues, and should not be applied chronically to wounds.[18-21] Instead, patients wishing to clean their wounds at home should do so with gentle soap and water. Other antiseptic preparations may be beneficial in appropriate situations. For example, a modified Dakin's solution at a concentration of 0.025% elicits antimicrobial effects without harming human tissues.[139] Similarly, cadexomer iodine, a complex of iodine with cadexomer (a modified starch-based polymer bead), can serve several important functions at the wound bed.[81] Cadexomer promotes the absorption of fluid, exudate, debris, and bacteria from the wound bed while facilitating the controlled release of iodine at levels that are not toxic to human cells.[81,140,141]

Silver ions have proven efficacy against commonly encountered wound pathogens, including Gram-negative bacteria and antibiotic resistant organisms like MRSA and vancomycin-resistant enterococci (VRE).[142-144] Silver ions kill bacteria by binding to and disrupting bacterial cell walls, damaging intracellular and nuclear membranes, poisoning respiratory enzymes, and denaturing bacterial DNA and RNA.[142,145] Although some species of bacteria (Pseudomonas in particular) have demonstrated resistance to certain silver preparations,[146] silver has a far lower propensity to induce bacterial resistance than classic antibiotics on account of its multi-targeted mechanism of action.[147]

Silver has been incorporated into a multitude of wound dressing products for prophylactic and therapeutic defense against potentially harmful organisms. Gauzes, hydrocolloids, alginates, foams, as well as creams, gels, and barrier layers are available with incorporated silver (Table IX). The various silver-containing dressings all possess a silver reservoir, but differ in the way in which the silver ions are released. Because silver ions, not silver atoms, produce the antimicrobial effects, silver must be present in a solution in order to exert its bactericidal properties.[142] Therefore, dry silver dressings require contact with wound moisture in order to release the active agent. In in vitro comparison studies, most silver-containing products exert some degree of bactericidal activity, though variation in the spectrum and rapidity of action exists.[144,148,149]

Disadvantages of silver products include potential irritation or discoloration of the surrounding tissues (argyria).[150,151] Additionally, in vitro studies suggest that silver may be toxic to keratinocytes and fibroblasts.[152,153] It is unclear if these findings are significant clinically, however, because in vivo studies have shown that silver-containing dressings actually accelerate wound healing.[154]

ADJUNCTS TO WOUND CARE
Compression

Compression therapy is considered the first-line treatment for venous ulcers. Numerous reports have indicated that compression therapy is superior to virtually any other type of dressing for the treatment of these wounds.[155-157] Compression relieves edema and stasis by reducing distention in superficial veins and assisting the calf muscle pump.[155] Compressive dressings also stimulate healthier granulation tissue.[158]

Because many patients with venous disease have concomitant arterial insufficiency, and because compression therapy in patients with undiagnosed arterial insufficiency can lead to ulcer worsening, gangrene, or limb amputation,[30,159] the caregiver must rule out clinically significant arterial disease before applying compression to a venous leg ulcer. A lower extremity with an ABI or TBI of 0.9 to 1.2 is considered normal and can generally be safely treated with compression. However, if the ABI is below 0.6 or the TBI is below 0.4, or either index is above 1.2 (suggesting noncompressible vessels), the clinician should seek consultation from vascular surgery before applying significant compression. Significantly increased pain on application of the compression dressing is a sign of arterial compromise in the bandaged limb, secondary to either iatrogenic overcompression or unrecognized underlying arterial disease; in either case, the dressing should promptly be removed. We often use light compression stockings to treat venous ulcers in cases where we suspect concomitant arterial disease. Uncompensated congestive heart failure is also a relative contraindication to compression therapy.

Compression may be administered in the form of single-layer bandages, multilayer bandages, compression stockings, or combinations of stockings and bandages (Table X). Bandages and stockings are classified according to the level of compression they apply to the limb. Although the optimal pressure necessary to overcome venous hypertension is not well defined, it is generally agreed that an external pressure of 35 to 40 mm Hg at the ankle is necessary to prevent capillary exudation in legs affected by venous disease.[157] Compression stockings, used both for the treatment of acute ulceration as well as for the prevention of ulcer recurrence, can provide up to 35 mm Hg of pressure at the ankle, and compression bandages can apply up to 60 mm Hg at the ankle, depending on the style of application.[157]

The Unna boot is a commonly used compression bandage (Fig 4) consisting of a zinc oxide–impregnated gauze wrap applied over the skin from the base of the toes to the popliteal flexure, covered with a layer of soft cotton, and wrapped with an elastic bandage that supplies compression. The zinc oxide protects the periwound skin and is thought to also enhance wound re-epithelialization and decrease inflammation.[160-162] Unna boots are typically left in place for 1 week, though they may need to be changed more frequently if the wound is especially exudative. Proper application of an Unna boot to supply the appropriate degree of pressure requires training and experience.

A Cochrane systematic review of 22 trials[157] found that compression therapy was more effective than noncompressive dressing types for the treatment of venous leg ulcers, and that high-compression systems were more effective than low-compression systems. There were no clear differences in the effectiveness of different high compression systems (eg, multilayer bandages, short-stretch bandages, or Unna boots). None of the included studies measured the amount of pressure applied by the bandages or stockings used, and therefore the actual dose–response relationship between compression and ulcer healing is unknown.

Once a venous ulcer has healed, it is critical to prevent recurrence. Relatively low pressure graded compression stockings that provide at least 30 mm Hg at the ankle are well suited to maintain intact skin. Because stocking elasticity decreases with time and washing, we encourage our patients to purchase two
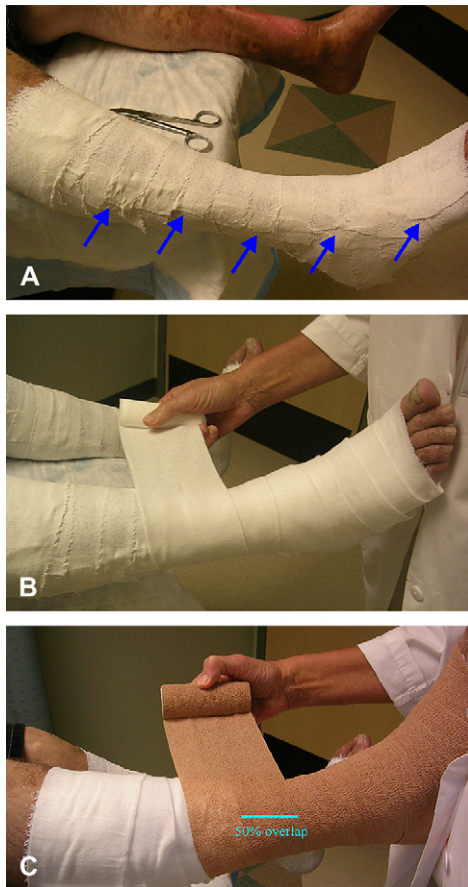
Fig 4. Unna boot application. **A**, Zinc oxide—impregnated gauze is wrapped around the limb, beginning at the base of the toes and extending to the popliteal flexure. Each time the limb is encircled, a pleat (see *arrows*) should be added to the dressing to accommodate potential future swelling. The foot should be held in 90° of dorsiflexion during dressing application. **B**, A soft cotton wrap is applied next. **C**, The elastic bandage layer supplies the compression. Each successive layer should have 50% overlap with the preceding layer.

pairs of stockings every 6 months to maintain appropriate pressure. Patients should also be encouraged to elevate their legs as often as possible to prevent ulcer recurrence.

Topical negative pressure devices

Topical negative pressure (TNP) devices, also known as vacuum-assisted closure (VAC) devices, consist of a fenestrated evacuation tube embedded in a foam dressing and covered with an airtight dressing. The tube is attached to a vacuum source, and subatmospheric pressure (100-125 mm Hg) is applied in a continuous or intermittent manner.[163] TNP dressings hasten wound healing by maintaining a moist environment, removing wound exudates, reducing bacterial loads, increasing local blood flow and granulation tissue formation, and applying mechanical pressure to promote wound closure.[163-167]

Current indications for TNP dressings include pressure ulcers, venous ulcers, and diabetic ulcers. TNP dressings are not appropriate for ischemic wounds because they may cause necrosis of the wound edges.[167,168] Wounds must be thoroughly debrided of all necrotic tissue before beginning therapy.[167,169] The foam component of the dressing should be changed every other day.[166,167] In some patients, dressing changes may be painful or cause trauma to the wound bed because of the ingrowth of new granulation tissue into the foam; the use of denser sponges and more frequent sponge changes can help alleviate this problem.[167]

A recent Cochrane review of the use of TNP devices for the treatment of chronic wounds found two small trials suggesting that TNP may increase the healing rate of chronic wounds compared to saline gauze dressings.[170]

Growth factors

Growth factors control many of the key cellular activities involved in the normal tissue repair process, including cell division, cell migration, angiogenesis, and synthesis of extracellular matrix components. Some have suggested that a deficiency of growth factors may exist in chronic wounds and investigators thus have examined the benefits of exogenous growth factor application for wound healing.[171] Recombinant human platelet—derived growth factor isoform BB (rhPDGF-BB homodimer, becaplermin; Regranex; Johnson & Johnson) is the only topical growth factor approved by the US Food and Drug Administration for the treatment of chronic wounds, indicated for use on chronic neuropathic lower extremity diabetic ulcers. The biologic activity of becaplermin is similar to that of endogenous PDGF-BB, that is, it promotes the chemotactic recruitment and proliferation of cells involved in wound repair.[172] Becaplermin clearly increases the probability that well perfused, properly debrided diabetic forefoot ulcers will heal completely and in shorter times.[173,174] It also appears to be beneficial for the treatment of pressure ulcers.[175-177]

Skin substitutes

In patients with serious recalcitrant ulcers, surgical skin grafting may be a treatment option. Grafting of split-thickness autologous skin is an established method of treating serious chronic venous leg ulcers. Allogenic and synthetic skin substitutes are now also available for the closure of longstanding wounds. Some such products have the advantage of eliminating the need for a graft donor site. Living skin

substitutes have shown benefits for the treatment of venous ulcers and diabetic neuropathic ulcers.[178-183] A comprehensive review of surgical options in wound management is beyond the scope of this paper.

Hyperbaric oxygen therapy

Hyperbaric oxygen therapy (HBOT) is occasionally used as an adjunct to standard wound care. HBOT, which involves breathing 100% oxygen at supra-atmospheric pressures while inside of a compression chamber, is based on the rationale that tissue hypoxia contributes to the failure of many chronic wounds to heal.[184] The benefits of HBOT for chronic wounds remain controversial.[185] Kranke et al[184] reviewed randomized controlled trials evaluating HBOT efficacy and reported that HBOT appears to decrease the rate of major amputation related to diabetic foot ulcers and may improve the chance of diabetic foot ulcer healing at 1 year. There was insufficient evidence to suggest benefits for venous, arterial, or pressure ulcers. In contrast, topical oxygen therapy, which involves inserting the wounded limb into an airtight bag and surrounding it with oxygen under slightly elevated pressure, is generally considered clinically ineffective.[186]

HBOT is associated with several potential adverse effects, including oxygen toxicity to brain and lung as well as barotrauma to the ears, lungs, and sinuses. In addition, temporary myopia is a very common adverse effect.[184] In order to minimize associated risks and costs, clinicians should attempt to confirm significant periwound hypoxia via transcutaneous oxygen measurements in candidate diabetic foot wounds before beginning therapy, in order to select wounds where a favorable treatment response would be most likely.[184]

Tretinoin

Paquette et al[187] report that "short-contact" daily application of topical tretinoin solution (0.05%) improved the healing of chronic leg ulcers in five patients by stimulating granulation tissue formation. Tom et al[188] then compared the effects of treatment with short-contact topical tretinoin versus placebo in 22 patients with diabetic foot ulcers, and demonstrated improved healing as well. In our own experience, application of small amounts of 0.025% tretinoin cream can precipitate neovascularization in ischemic wound beds. Because tretinoin may cause irritation, erythema, and/or burning, however, application should avoid the periwound skin.

Pentoxifylline

In patients with venous leg ulcers that persist despite compression therapy, oral pentoxifylline may be a viable treatment adjunct. A Cochrane systematic review of nine trials[189] determined that pentoxifylline plus compression produces superior ulcer healing than placebo plus compression. These benefits may be caused by pentoxifylline's fibrinolytic properties,[190] antithrombotic effects,[191,192] and/or inhibition of the production of proinflammatory cytokines.[193,194]

GLOBAL APPROACH TO WOUND CARE

The treatment of patients with chronic wounds requires a team approach. There must be a partnership between the patient, the patient's family, the medical team, and outpatient support agencies, with clear communication and an understanding of the fundamentals of care between all individuals. Even the most expert wound care team will fail if communication with the patient and the patient's family is faulty. In order to be successful, there must also be knowledgeable collaboration between wound care specialists (both physicians and nurses), dermatologists, geriatricians, surgeons, and primary care physicians.

To meet the communication goals we need audience-appropriate educational materials for healthcare workers as well as patients. Educational materials must be culturally relevant, because there are major regional differences in family dynamics, outpatient support systems, financial circumstances, and approaches to the elderly within the United States. Such differences are even more profound internationally. Nevertheless, there are certain universal core principles that can be incorporated into clearly articulated documents which can be modified depending on culture, language, and historical precedence.

CONCLUSION

Medicine generally and dermatology specifically must place great emphasis on quality wound care. In order to remedy the dearth of wound care expertise among physicians in the United States, we must modify how we teach medical students, residents, and colleagues. We are in major need of evidence-based wound care. Often, wound therapy is anecdotal and predicated upon the "dressing of the month." Medicine must establish suitable protocols that allow us to quantifiably determine which materials are effective in facilitating wound healing while remaining cost effective. The costs of wound care are escalating dramatically, and as our population ages, the incidence of chronic wounds will almost certainly increase. The staggering expenditures presently extant do not even quantify the loss of productivity, deleterious effects of wounds on quality of life, or the indirect costs incurred by voluntary

caregivers in time and effort spent caring for patients. Medical dermatology has a major responsibility to shape the future of care for skin ulcers.

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